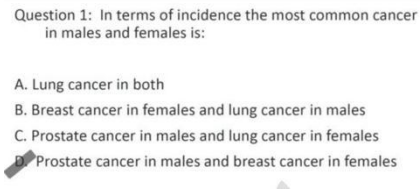
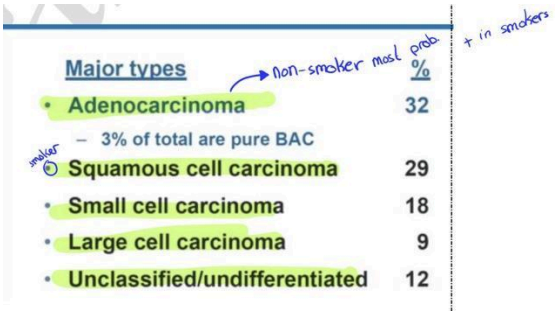
🫁 1. Epidemiology & Etiology

Etiology of Lung Cancer (risk factors):

- 🚬 **Tobacco:** Causes 80-90% of lung cancer cases.
  - o 📈 Clear dose-response relationship.
  - o 💨 Passive smoking may cause up to 25% of lung cancer in non-smokers (2.5–5% of all cases).
- 🧬 **Genetic Susceptibility:**
  - o 10–15% of active smokers develop lung cancer.
- ☢️ **Other Causes:**
  - o Environmental & Occupational Exposures: Asbestos, radon, polycyclic hydrocarbons, cadmium, chloromethyl ether, chromium, nickel, arsenic.
- 🎂 **Age:**
  - o Risk increases with age; the average age at diagnosis is 70.
- 😮‍💨 **COPD:**
  - o Increases lung cancer risk 3–6x more than smoking alone.





🧬 2. WHO Classification of Lung Cancer

Types of Lung Cancer

1. 🧱 **Squamous Cell Carcinoma:**
   - o 95% are smokers, centrally located, can cavitate.
   - o Associated with HPO (hypertrophic pulmonary osteoarthropathy) and hypercalcemia.
2. 🧪 **Adenocarcinoma:**
   - o Most common histologic subtype.
   - o Increased incidence in never-smokers.
   - o Peripheral and metastatic.
3. 🔬 **Small Cell Lung Cancer (SCLC):**
   - o Almost all cases occur in smokers.
   - o Central, metastatic at presentation.
   - o Associated with paraneoplastic syndromes (other than hypercalcemia).

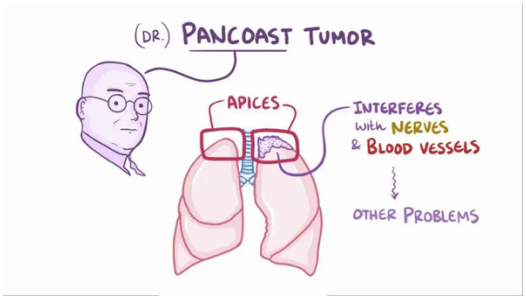
🔍 3. Pathology of Lung Cancer

Adenocarcinoma Pathology

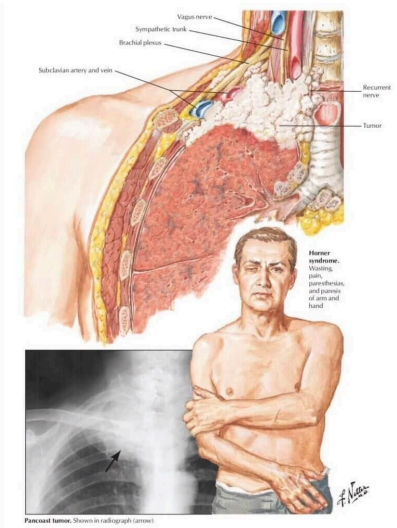
- Neoplastic gland formation, pneumocyte marker expression (TTF-1, napsin) or intracytoplasmic mucin.
- Subtypes:
  - o Mucinous vs. Nonmucinous (acinar, papillary, micropapillary, lepidic, solid).
  - o Adverse prognostic patterns: Solid, micropapillary, cribriform (a subtype of acinar nonmucinous adenocarcinoma).
  - o Minimally invasive adenocarcinoma (MIA): ≤3 cm, ≤5 mm invasion, predominant lepidic growth pattern.
  - o Lepidic-predominant adenocarcinoma: Invasion >5 mm.

Squamous Cell Carcinoma Pathology

- Defined by keratin and/or intercellular desmosomes.
- Identified via immunohistochemistry (IHC): p40, p63, CK5, CK5/6, desmoglein.
- Subtypes:



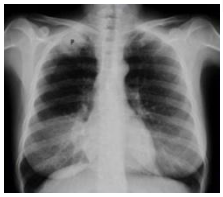
o Nonkeratinizing, Keratinizing, Basaloid.
• Key Features:
o Central necrosis with resulting Cavitation, Pancoast tumors, Hypercalcemia.
o Brain is the most common site of recurrence.
o Pancoast Tumor Symptoms: Shoulder pain (96%): The pain could potentially be secondary to the invasion of brachial plexus, pleural invasion, extension into ribs or vertebral bodies, and is generally progressive.
o Horner's Syndrome: Ipsilateral ptosis, miosis, anhidrosis due to invasion of sympathetic trunk



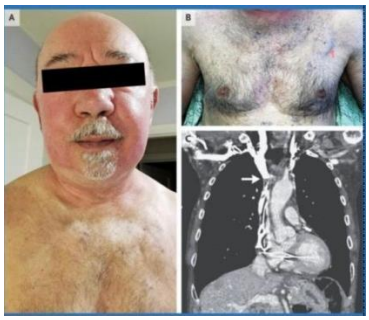
Pancoast tumor. Shown in radiograph (arrow)

🩺 4. Diagnosis & Symptoms

Common Symptoms
• Cough (75%), Dyspnea, Chest pain, Hemoptysis (15-30%).
• Less Common Symptoms:
o Clubbing, Hoarseness, Dysphagia, Wheezing.
o 15% present with pleural effusion.
o 5-15% are asymptomatic.
• 15% present with extra-pulmonary symptoms.
• 5% may present with a paraneoplastic syndrome.
• Cancer symptoms: new onset wt loss, headaches, bone pain.



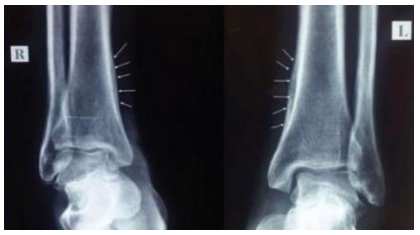
Superior Vena Cava (SVC) Syndrome
• Common in SCLC.
• Symptoms:
o Dilated neck veins, facial and upper extremity edema, plethoric appearance.
o CXR shows mediastinal widening or right hilar mass.



⚠️ 5. Paraneoplastic Syndromes Associated with Lung Cancer

Hypercalcemia
• Caused by PTHrP secretion or bony metastases.
• Symptoms: Anorexia, nausea, constipation, lethargy.

SIADH (Syndrome of Inappropriate ADH Secretion)
• Associated with SCLC, leads to hyponatremia.



Neurologic Paraneoplastic Syndromes (SCLC-Related)
• Immune mediated syndromes
• Lambert-Eaton Myasthenic Syndrome (LEMS).
• Encephalomyelitis, Limbic encephalitis, Cerebellar ataxia.
• Sensory & Autonomic Neuropathy.

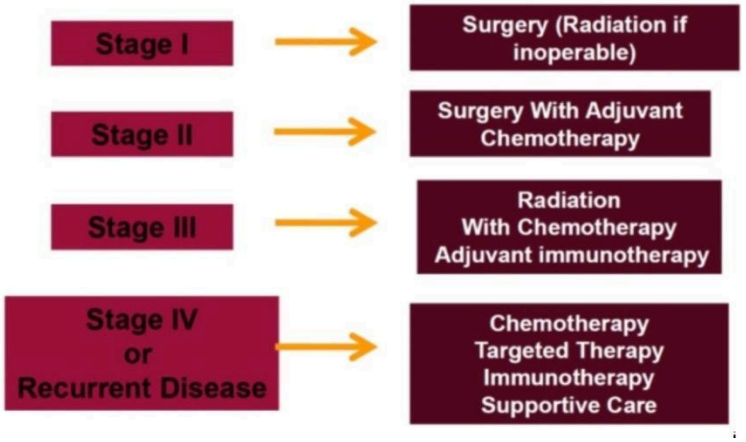
Ectopic ACTH Production
• Causes Cushing's Syndrome, associated with SCLC, large-cell neuroendocrine carcinoma, and carcinoid tumors.

Hypertrophic Pulmonary Osteoarthropathy (HOA)
• Clubbing, periosteal activity of tubular bones, joint effusion, arthralgias. Characterized by abnormal proliferation of the skin, soft tissues, and osseous tissues in the distal parts of extremities.

Dermatomyositis and polymyositis

🫁 6. Evaluation & Staging

Evaluation Guidelines
• Goal: Timely diagnosis and accurate staging.
• ACCP guidelines:
  o Initial evaluation should be completed within six weeks for patients with tolerable symptoms.
• Diagnosis by Stage:
  o Stage I & II: Diagnosed in 26% and 8% of cases.
  o Stage III & IV: Diagnosed in 28% and 38%, respectively.



Imaging & Invasive Staging
• Radiological Staging:
  o Contrast-enhanced CT (chest + upper abdomen).
  o PET scan for metastases.
  o MRI brain for tumors >5 cm.
• Invasive Staging:
  o EBUS-TBNA (Bronchoscopic endobronchial ultrasound-transbronchial needle aspiration), Endoscopic-TBNA, Mediastinoscopy, VATS.

In patients who do not have the pulmonary reserve to tolerate pneumonectomy or lobectomy, a more conservative approach with **wedge resection or segmentectomy** can be done.
●The disadvantage is **a higher local recurrence rate**, but survival is the same.

📊 7. Staging

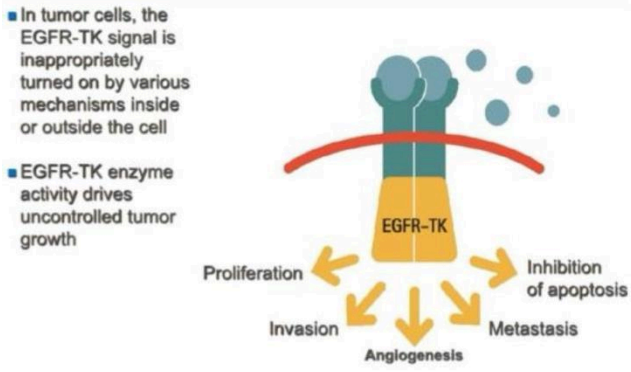
TNM Classification:
• T: Tumor size and local invasion.
• N: Lymph node involvement.
• M: Metastasis presence.
Importance: Determines treatment approach and prognosis.

💉 8. Treatment

Two Main Questions:
• Is the tumor resectable (staging)?
• Is the patient operable (general health)?

Non-Small Cell Lung Cancer (NSCLC)
• Stage I:
  o Surgery (lobectomy or pneumonectomy) with mediastinal lymph node sampling.
  o 5-year survival: IA (78%), IB (53%).
• Stage II:
  o Surgery + adjuvant chemotherapy.
  o Chest wall invasion → en-bloc resection of chest wall.
• Stage III:
  o Stage IIIA (N1 nodes): Surgery if resectable.

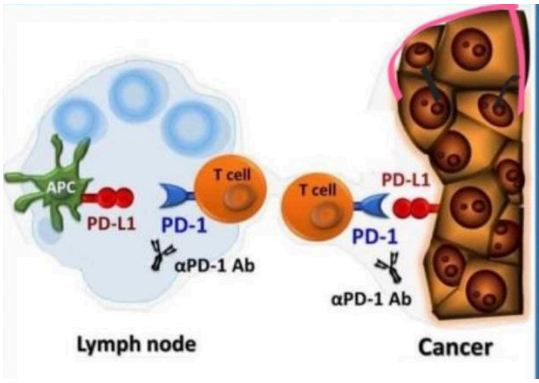
Pancoast tumor is a unique tumor of stage II. It arises from the superior sulcus and is usually diagnosed at a higher stage IIB or IIIA



o Stage IIIA (N2/N3): Concurrent chemo-radiotherapy.
o Stage IIIB: Unresectable, chemo-radiotherapy ± surgery.
• Stage IV:
o Palliative chemotherapy, low survival (5-year survival 1–3%).

Small Cell Lung Cancer (SCLC)
• Limited Stage (LS-SCLC):
o Stage 1 (no lymphadenopathy): Lobectomy + adjuvant chemotherapy.
o Mediastinal/hilar involvement: Chemo + radiation.
o Whole-brain prophylactic radiation (reduces metastasis risk).
• Extensive Stage (ES-SCLC):
o Distant metastasis, malignant pleural or pericardial effusions, contralateral hilar or supraclavicular lymph node involvement
o Platinum-based chemotherapy.
o Radiation + whole-brain irradiation (for remission cases).
o Median survival: 8–13 months.

🧪 9. Advanced Therapies



Targeted Therapy
• EGFR mutation: Inhibited by tyrosine kinase inhibitors: Erlotinib, Gefitinib, Afatinib.
• ALK/ROS1 Inhibitors: Crizotinib, Ceritinib, Alectinib.

Immunotherapy
• PD1 plays an important role in downregulating T cells and promoting self-tolerance.
• Tumors that lack a targetable mutation or fail targeted therapy may benefit from immune checkpoint inhibitors.
• PD-1 inhibitors: Nivolumab, Pembrolizumab (for PD-L1 >50% expression).
• VEGF-A Inhibitor (Bevacizumab): Used in non-squamous NSCLC, contraindicated in squamous NSCLC.
• In patients unfit for pneumonectomy or lobectomy:
o Wedge resection or segmentectomy (higher local recurrence, same survival).

🧪 10. Lung Cancer Screening

• 20% reduction in lung cancer mortality with low-dose CT (LDCT).

📝 TEST BANK

1. A 62-year-old gentleman who is a smoker with 26 pack-years came to the clinic complaining of recent onset hemoptysis & hoarseness. He has also had significant unintentional weight loss over the past month. Chest x-ray reveals an upper large mass in the right lung with cavitation. Lab studies show elevated Ca+2.
What is the most likely diagnosis?
a. Squamous cell carcinoma
b. Adenocarcinoma
c. Small cell lung carcinoma
d. Sarcomatoid carcinoma

e. Neuroendocrine carcinoma
Answer: a. ✅ Squamous Cell Carcinoma is most likely because the patient is a heavy smoker, has a central cavitary lung mass, presents with hemoptysis, hoarseness, and has elevated calcium — all classic features of SCC.

- **2.** All of the following are true about small cell lung carcinoma (SCLC) EXCEPT:
  a. It is the most common cause of malignancy-related SIADH
  b. It is associated with Pancoast tumour
  c. Cushing syndrome is common in patients with SCLC
  d. It is very responsive to chemotherapy
  e. It is the most common cancer associated with paraneoplastic neurologic syndromes
  Answer: b. Pancoast tumors are typically apical lung tumors that invade local structures like the brachial plexus and sympathetic chain (→ Horner's syndrome).
  These are classically caused by non-small cell lung cancers, especially squamous cell carcinoma or adenocarcinoma — NOT SCLC.